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Current view

Assessing quality of life in medical trials on patients with inflammatory bowel disease

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INTRODUCTION

Over the past two decades, health-related quality of life (HRQOL) has developed from an obscure and speculative notion to a concrete index of health status. Today, HRQOL as an index of subjective health status can reliably be measured. It has been defined as "a global measure of the patient's perceptions, illness experience, and functional status that incorporates social, cultural, psychological, and disease-related factors"[1]. HRQOL is being used in evaluating therapeutic interventions and in facilitating health-care planning in many chronic diseases.

Inflammatory bowel disease (IBD) has an important impact on HRQOL. As long as the endpoint of the management of IBD is identified with the greatest possible reduction of the impact of the disease on general well-being, it is of particular importance to perform measurements of quality of life in a reliable and prospective manner. Qualitative and semi-quantitative measurements of HRQOL were mainly used in the past. In a review on quality of life assessment in all illnesses, that dates from 1987, 95% of all surgical trials reviewed used qualitative and semi-quantitative methods in a retrospective design.[2] This situation has now changed in favor of randomized, controlled and prospective trials, both surgical and medical, using reliable HRQOL instruments.

Medical trials on IBD patients using HRQOL as an outcome measure, are less numerous than surgical ones. This is understandable, as surgical treatment represents a major health intervention compared to medical therapies. The fact that medical studies that used HRQOL as an outcome measure began about a decade after the first surgical ones, brings with it an important advantage: most of the medical trials have used high standards regarding study design and quality-of-life instruments.

In this review we will examine studies that considered HRQOL as an outcome measure in medical treatments in IBD patients, which were designed with high standards and used valid and reliable instruments.

METHODS

A search of the Medline database since 1980 was made for articles referring to ulcerative colitis, Crohn's disease, inflammatory bowel disease, quality of life, and medical treatment. Studies using only qualitative "methods" for QoL assessement were thought to give little or unreliable information about the effects of intervention on HRQOL, and so were excluded. Articles that made no direct measure of HRQOL, did not concern adults, did not refer to IBD and were not published in peer-reviewed journals were also excluded.

Assessment of HRQOL with valid instruments in medical studies on IBD patients

Nyman et al studied prospectively the clinical effects of long-term treatment with azatioprine or 6-mercaptopurine in 42 patients with severe Crohn's disease and extensive colonic involvement. The treatment period was 5 years. The authors used a 3-scale quality-of-life instrument and there was no control group.[3]

Irvine et al used the IBDQ in a prospective, double blind, placebo controlled study of cyclosporine in 305

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patients with stable Crohn's disease. The study was also used for further validation of IBDQ in Crohn's disease patients. IBDQ scores correlated highly with CDAI ($r=0,67$; $p<0,0001$). IBDQ scores were lower in patients who required surgery. Furthermore, IBDQ results predicted the group that would undergo surgery, even when disease activity scores did not.[4]

IBDQ was used in another multicenter, randomized, prospective, placebo-controlled trial of budesonide for active Crohn's disease. In a double-blind design, 258 patients were randomly assigned to receive placebo or one of three dosage schedules of budesonide 3, 9, or 15 mg daily. Clinical activity (as measured by CDAI) showed similar improvements with 9 mg daily and 15 mg daily (both regimens ran better than 3 mg and much better than placebo). IBDQ scores showed a better improvement at 9 mg daily than 15 mg daily. In this study, the assessment of HRQOL helped in determining the best dosage schedule for the patients.[5]

In a double-blind, placebo-controlled, randomized, parallel trial, Singleton et al used an instrument developed for measuring the effects of mesalamine on quality of life in patients with Crohn's disease. Seven quality-of-life parameters were assessed: ability to sleep throughout the night, sexual relationship, performance of routine outdoor activities, indoor (other than sleep) activities, social activities, work and occupational activities, hobbies and recreational activities. A horizontal visual analogue scale ranging from 0 (no effect) to 10 ("as bad as it can be") was used. The instrument was tested for validity, reliability, and responsiveness using CDAI as a primary end point for efficacy analysis. Results revealed that mesalamine at the dose of 4 mg daily resulted in significant improvements in all quality-of-life parameters ($p<0,03$). A significant ($p<0,02$) linear trend between increasing doses and increasing response was also noted.[6]

In a study comparing budesonide versus prednisone in active Crohn's disease involving the terminal ileum and the colon, quality of life was assessed along with Crohn's Disease Activity Index (CDAI), a disease activity index developed for Crohn's disease. Patients on budesonide scored better in matters of quality of life, having fewer adverse reactions than patients treated with prednisone. Twice as many in the budesonide group responded to treatment with no side effects compared with the prednisone group (30% vs. 14%) The instrument for the assessment of HRQOL used was the IBDQ.[7]

Rutgeerts et al[8] evaluated the HRQOL of 73 patients with active CD in a randomized, double-blind, placebo-controlled trial where an anti-tumor necrosis factor monoclonal antibody (Infliximab) was tested. Based on analyses of the Inflammatory Bowel Disease Questionnaire (IBDQ, a disease-specific, quality-of-life index) scores and CDAI scores, as well as serum CRP concentrations, the group receiving Infliximab demonstrated continued or improved suppression of disease activity at levels associated with disease remission (IBDQ scores above 170).

Patients with Crohn's disease receiving home parenteral nutrition, had a reduced quality of life when compared to anatomical or functional short bowel counterparts not receiving parenteral nutrition. The levels of quality of life measured were similar to those reported for patients with chronic renal failure treated by dialysis. The instruments for the quality of life assessment were the IBDQ and the Sickness Impact Profile, a non-disease-specific quality of life questionnaire.[9] In another study dealing also with quality of life in patients treated with home parenteral nutrition, among them 35 with Crohn's disease, the health status of the young patients was good compared with the normal population, whilst the poorest scores were in older patients and those receiving narcotic drugs. The instruments for the HRQOL assessment were the Short Form 36 and the EuroQoL, two non-disease-specific instruments. The EuroQoL utility scores confirmed the Short Form 36 results.[10]

Somerville et al used a visual analogue scale measure of HRQOL of several domains of quality of life in order to compare hydrocortisone foam to prednisolone enemas, in 46 patients with exacerbation of UC. Validation of this instrument is not included in the study. Clinical symptoms and endoscopic picture showed similar improvement with both treatments, but in several domains of HRQOL (e.g. sexual function, occupational activity, work activity, routine outdoor activity) hydrocortisone foam was significantly superior to prednisolone.[11]

Quality of life was evaluated in 374 ulcerative colitis patients using controlled-release mesalamine capsules (Pentasa) with dosage schedules of 1g, 2g, and 4g daily versus placebo, during 8 weeks, in a randomized, placebo-controlled, double-blind, multicentre trial by Robinson et al. In this study, function-related quality of life parameters were assessed, including five pertinent clinical symptoms and seven general life capabilities. This instrument had been previously shown to be valid, reliable, and sensitive to change in ulcerative colitis patients. All of the parameters were recorded using a 10-cm visual analogue scale and trips to the toilet were recorded in

patients diaries. Mesalamine dosage schedules of 2g and 4g daily were significantly superior to placebo in improving each of the 12 quality-of-life parameters ($p<0.05$). These results indicate that controlled-release mesalamine significantly enhances the quality of life for patients with either left-sided ulcerative colitis or pancolitis.[12]

A recent publication dealt with the quality of life in patients with severe, steroid refractory UC under medical treatment with intravenous cyclosporin compared to total colectomy, the two groups consisting of 18 and 46 patients respectively. The IBDQ and two visual analogue scales were used. Patients under cyclosporin had a better ability to sleep, better stool consistency, less abdominal or rectal pain and fewer visits to the toilet. Surgical patients paid fewer visits to their specialists and used less medication. In general, patients with severe UC treated with intravenous cyclosporin scored as well as or better than surgical patients.[13]

CONCLUSIONS

A general conclusion from the above presented studies is that the assessment of HRQOL represents a major achievement in the management of IBD patients. More precisely, using a HRQOL instrument, a significant difference between two conservative enema treatments in UC relapses emerged. This difference could not have been found if only clinical and endoscopic improvement had been used as an instrument of assessment.[11] Furthermore, measuring the HRQOL, both the usefulness of mesalamine and the best dosage schedule in UC patients could be objectively estimated.[12] Finally, quality of life assessment with valid instruments in patients with severe, steroid-refractory UC treated with cyclosporin revealed scores equal or better than those of patients after total colectomy.

Measuring HRQOL in an objective and reliable way is considered as a prerequisite of well-designed IBD medical trials and will be increasingly important in the future. Specific instruments for HRQOL assessment that have been previously validated should be used, in order to facilitate comparability between trials.

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